Medical Diagnostic X Rays and Thyroid Cancer

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Background: Diagnostic x rays are the largest man-made source of exposure to ionizing radiation for the general population. Whether there are meaningful cancer risks associated with such exposures is unclear. Most previous casecontrol studies have relied on recalled histories of x rays, and there is concern that completeness and accuracy of recall might differ between cancer case and control subjects. Purpose: The present study used information recorded prospectively in hospital charts to address the relationship between medical diagnostic x rays and risk of thyroid cancer. Methods: The Swedish Cancer Registry and the Uppsala-Örebro Regional Cancer Registry were used to identify persons with papillary or follicular thyroid cancer diagnosed from January 1, 1980, through December 31, 1992, among residents of the Uppsala Health Care Region. After histopathologic review, there were 484 such case subjects available for study. An equal number of age-, sex-, and county of residence-matched control subjects from the general population were randomly selected on the basis of the Swedish Registry of the Total Population. Lifetime residential histories were compiled, and radiology records were searched at all Swedish hospitals serving regions where study subjects ever maintained an official residence. Approximate radiation doses to the thyroid gland for specific types of x-ray examinations were assigned on the basis of mean values of measurements made in Sweden in 1973-1975 and in the United States in 1970. Odds ratios were used to evaluate the association between diagnostic radiography and risk of thyroid cancer. Results: A total of 3853 medical diagnostic x rays were ascertained among thyroid cancer case subjects and 4039 among the matched control subjects. There was no tendency for case subjects to have had more of the types of x-ray procedure associated with higher radiation dose to the thyroid gland (i.e., those involving the head or neck area). This finding was true even when analysis was restricted to x rays occurring before 1960, when doses likely were higher than in more recent years, and for examinations occurring in childhood and adolescence, when susceptibility to radiation-induced thyroid cancer is greatest. The relative risk of thyroid cancer was not significantly associated with estimated cumulative dose to the thyroid gland from diagnostic x rays (two-sided P for trend = .80). Conclusion: These data indicate that the risk of thyroid cancer due to medical diagnostic x rays, if any, is very small. [J Natl Cancer Inst 1995;87:1613-21]

Diagnostic radiology is the largest man-made source of exposure to ionizing radiation for the general population (1,2). Except for unusual circumstances in years past, such as repeated chest fluoroscopies in tuberculosis patients (3), cancer risks attributable to diagnostic irradiation are believed to be very small (4,5). However, studies have reported elevated risks of chronic myeloid and monocytic leukemia, meningioma, glioma, parotid gland tumors, and thyroid cancer associated with diagnostic medical and dental x rays, especially for high-dose exposures that occurred several decades ago (6-10). Given the high prevalence and frequency of exposure to diagnostic x rays, any measurable increase in cancer risk would be of considerable public health importance.

An important limitation of most previous studies (6-10) was the use of interviews to reconstruct histories of exposure. A study by Graham et al. (11) indicated that reliance on interview data alone resulted in substantial underascertainment of diagnostic x rays, and the possibility of differential recall of x rays by case and control subjects usually cannot be ruled out. Errors associated with incomplete or inaccurate recall can be avoided by ascertaining exposure through medical records rather than

Subjects and Methods

This case—control study was made possible by unique features of the Swedish health care system. At the time of the study, the public medical service in Sweden was divided into 27 financially and administratively independent areas: 25 counties and two cities. Within these areas were the following three categories of hospital: 1) regional hospitals, of which there were 10 (one for each region—a region contains one or more administrative areas); 2) central hospitals, of which there were 23 (generally one per county but, in some instances, the regional hospital served a dual role as central and regional hospital); and 3) community hospitals, of which there were 64 (one to several per county). All individuals resident in a given area were served by at least one such hospital; for those served by a community hospital, the central hospital served as the primary referral center. Highly specialized medical services were provided to several counties by a regional hospital. Charges for medical services were kept low enough to permit all citizens equal access to health care. Only in an emergency

Specific types of x-ray examinations were assigned approximate doses based on mean values of measurements made in 1973-1975 in Sweden (17) and in 1970 in the United States (18) (Table 1). The Swedish data were used preferentially, if available. These values should not be assumed to accurately represent the dose for an individual from any single examination. Some of the estimates are based on small numbers of dose measurements and are subject to considerable uncertainty. Factors such as field sizes, angles of projections, and numbers of films could not be taken into account. Also, duration of exposure and extent of exposed area were not available for fluoroscopic examinations of the upper gastrointestinal tract. Finally, doses from diagnostic radiography have declined over time, and measurements from one era are not applicable to all time periods. We were not able to locate information by which to quantify this secular trend. The objective here was to sort case subjects and control subjects into ordinal categories based on cumulative radiation dose, not to estimate exact doses for individuals. More than three quarters of the x rays of case subjects and control subjects occurred during the 1960s or 1970s (see below), so the measurements of Bengtsson et al. (17) and Kereiakes and Rosenstein (18) are relevant to the time period in which most x rays of study subjects occurred.

Odds ratios were used as estimators of RR. Conditional logistic regression models (19-21) were used to estimate RRs and associated 95% confidence intervals (CIs) and to test for trend in the RR. Estimates and tests are based on likelihood methods. All P values resulted from two-sided tests. Only x-ray examinations that occurred 5 or more years before the date of thyroid cancer diagnosis for the case or matched control subject were included in these analyses, because radiation-induced thyroid cancers rarely are detected until at least 5 years after the relevant exposure (2).

Table 1. Average thyroid doses for common radiographic examinations in Sweden and the United States, based on surveys conducted in the 1970s*

| | Thyroid dose, mGy | | | |
|-------------------------------------|-------------------|----------------|--|--|
| Examination | Sweden† | United States‡ | | |
| Lungs (full size), ribs | 0.17 | | | |
| Lungs (photofluorography) | 1.00 | | | |
| Lungs plus heart | 0.24 | | | |
| Chest | | 0.065 | | |
| Ribs | | 1.54 | | |
| Head, sinus | 7.90 | | | |
| Skull | | 2.22 | | |
| Cerebral angiography | 3.00 | | | |
| Shoulder, clavicle, sternum | < 0.50 | | | |
| Shoulder (one) | | 0.58 | | |
| Arm | < 0.01 | | | |
| Cervical spine | 1.40 | 4.04 | | |
| Thoracic spine | 13.0 | 0.75 | | |
| Lumbar spine | 0.16 | 0.003 | | |
| Lumbosacral spine | <0.01 | 0.0005 | | |
| Full spine (chiropractic) | | 2.71 | | |
| Pelvis | < 0.01 | < 0.0001 | | |
| Hip and upper femur | < 0.01 | < 0.0001 | | |
| Pelvimetry | < 0.10 | | | |
| Hysterosalpingography | < 0.01 | | | |
| Abdomen | 0.03 | | | |
| KUB (i.e., kidney, ureter, bladder) | | 0.0001 | | |
| Stomach and duodenum | 0.29 | | | |
| Upper gastrointestinal tract | | 0.070 | | |
| Small intestine | 0.03 | | | |
| Colon | 0.10 | | | |
| Barium enema | | 0.002 | | |
| Cholecystography/cholangiography | 0.03 | 0.010 | | |
| Urography | 0.38 | | | |
| Retrograde pyelography | 0.50 | | | |
| Intravenous pyelogram | | 0.0001 | | |
| Urethrocystography | 0.05 | | | |
| Dental (intraoral, single exposure) | 0.03 | | | |

^{*}Categories used are as reported in the source publications.

The study was conducted with the approval of the institutional review board at University Hospital in Uppsala.

Results

Three hundred fifty-seven (74%) of the 484 case subjects had papillary carcinoma, and 127 (26%) had follicular carcinoma. The mean age at diagnosis was 51.5 years for papillary carcinoma, 62.7 years for follicular carcinoma, and 54.4 years overall. Three hundred seventy-one (77%) of the case subjects were female. A female predominance was seen at all ages, but it was more pronounced at the younger ages (85% of case subjects under the age of 40).

A total of 7892 x-ray examinations were ascertained (Table 2), of which 6148 (78%) occurred 5 or more years before the date of thyroid cancer diagnosis. The earliest recorded x ray was given in 1934. Nearly half of the procedures occurred in the 1970s. Excluding the 5 years before diagnosis, case subjects had received an average of 6.1 documented medical x-ray procedures of all types in their lifetimes; the corresponding number for control subjects was 6.6. Maximum numbers of x-ray examinations for individual case and control subjects were 76 and 95, respectively. For 97 case subjects (20%) and 98 control subjects (20%), no radiology record documentation of ever having received diagnostic x rays was found. These numbers increased to 115 (24%) and 117 (24%), respectively, when x rays received during the 5 years preceding the date of thyroid cancer diagnosis were excluded.

Table 3 shows the numbers of case and control subjects ever exposed to specific types of radiographic examinations as well as the mean and maximum numbers of examinations among

Table 2. Number of medical x-ray examinations of all types among 484 thyroid cancer case subjects and an equal number of age- and sex-matched population control subjects

| TD' ' | Total No. of x-ray examinations | | | |
|--------------------------------------|---------------------------------|------------------|--|--|
| Time interval or population subgroup | Case subjects | Control subjects | | |
| Total | | | | |
| All years | 3853 | 4039 | | |
| ≥5 y before diagnosis of case | 2937 | 3211 | | |
| Sex* | | | | |
| Females $(n = 371)$ | 2255 | 2457 | | |
| Males (n = 113) | 682 | 754 | | |
| Calendar year of examination* | | | | |
| <1950 | 33 | 73 | | |
| 1950-1959 | 265 | 290 | | |
| 1960-1969 | 906 | 1043 | | |
| 1970-1979 | 1368 | 1459 | | |
| 1980-1987 | 365 | 346 | | |
| Age at examination, y* | | | | |
| <20 | 272 | 237 | | |
| 20-39 | 947 | 1079 | | |
| 40-59 | 1153 | 1289 | | |
| ≥60 | 565 | 606 | | |
| Year of thyroid cancer diagnosis* | | | | |
| 1980-1985 | 1341 | 1628 | | |
| 1986-1992 | 1596 | 1583 | | |

^{*}Excluding x rays that occurred within 5 years before diagnosis of thyroid cancer in the case subjects and matched control subjects.

[†]From Bengtsson et al. (17). Sample sizes for some procedures are very small, and dose estimates among individual patients varied considerably.

[‡]From Kereiakes and Rosenstein (18).

Table 3. Numbers of case and control subjects ever exposed to specific radiographic examinations and mean and maximum number of examinations per exposed person*

| | Case s | subjects (n= 484) | Control subjects (n = 484) | | |
|--|----------------|---|----------------------------|---|--|
| Examination | No. exposed | Examinations per exposed person, mean (maximum) | No. exposed | Examinations per exposed person, mean (maximum) | |
| Head and neck | | | | | |
| Orbits | 3 | 1.33(2) | 3 | 1.00(1) | |
| Mandible/jaw | 12 | 1.42(3) | 4 | 2.00(3) | |
| Nasal bones/sinuses | 48 | 1.46 (5) | 58 | 1.53 (4) | |
| Other bones of face | 4 | 1.25 (2) | 12 | 1.58 (4) | |
| Skull | 30 | 1.47 (8) | 34 | 1.53 (6) | |
| Teeth, partial† Teeth, full mouth† | 1 6 | 1.00(1) | 2 | 1.00(1) | |
| Neck for soft tissues | 47 | 1.33 (3) 1.28 (5) | 0 20 | 1.40(3) | |
| Computed tomography scan, head | 2 | 1.00(1) | 0 | 1.40(3) | |
| Other (head) | 2 | 2.50 (4) | 4 | 1.00(1) | |
| Head/neck, not otherwise specified | 0 | | i | 1.00(1) | |
| Cerebral/carotid arteriogram | 1 | 1.00(1) | 1 | 1.00(1) | |
| Any examination of head/neck | 110 | 1.97 (11) | 102 | 2.03(7) | |
| Chest and shoulder | | | | | |
| Chest, radiograph | 217 | 3.22 (23) | 202 | 3.69 (68) | |
| Chest, photofluorograph | 195 | 2.21 (7) | 213 | 2.53 (14) | |
| Chest, fluoroscopic | 1 | 2.00(2) | 1 | 1.00(1) | |
| Heart, plain film | 2 | 1.00(1) | 0 | | |
| Computed tomography scan, chest | 3 | 1.67 (3) | 4 | 1.00(1) | |
| Ribs | 13 | 1.46(2) | 12 | 1.25(2) | |
| Mammogram | 7 | 1.43 (3) | 2 | 1.50(2) | |
| Other (chest) | 0 | | 2 | 1.00(1) | |
| Clavicie Scapula | 3 | 1.00(1) | 2 | 1.00(1) | |
| Shoulder | 2 33 | 1.50(2) | 7 40 | 1.57 (4) | |
| Any examination of chest/shoulder | 320 | 1.61 (7) 3.82 (26) | 314 | 1.58 (7) 4.41 (69) | |
| | 320 | 3.02 (20) | 314 | 4.41 (07) | |
| Spine and pelvis Full spine | 10 | 1.10(2) | 0 | | |
| Cervical spine | 10 42 | 1.10(2) | 9 | 1.11 (2) | |
| Cervical spine Cervicothoracic spine | 5 | 1.29 (3) 1.00 (1) | 45 12 | 1.27 (3) | |
| Thoracic spine | 7 | 1.00(1) | 3 | 1.08 (2) 1.00 (1) | |
| Thoracolumbar spine | 22 | 1.23 (4) | 25 | 1.12(2) | |
| Lumbar spine | 39 | 1.26 (3) | 59 | 1.25 (4) | |
| Lumbosacral spine | 24 | 1.21(2) | 22 | 1.18(3) | |
| Sacrum and coccyx | 8 | 1.63 (6) | 16 | 1.12(2) | |
| Pelvis | 38 | 1.61 (9) | 53 | 1.62(8) | |
| Myelogram | 4 | 1.25 (2) | 4 | 1.25(2) | |
| Any examination of spine/pelvis | 112 | 2.33 (18) | 131 | 2.44 (12) | |
| Arms and hands | | | | | |
| Humerus, upper arm | 5 | 1.00(1) | 5 | 1.80(4) | |
| Elbow | 13 | 1.69 (7) | 20 | 1.25 (4) | |
| Forearm, radius, ulna | 4 | 2.50 (4) | 7 | 2.14 (6) | |
| Hand, wrist, finger(s) Any examination of arms/hands | 67 78 | 2.93 (10) | 83 | 3.24 (21) | |
| • | 76 | 2.99 (10) | 100 | 3.18 (21) | |
| Lower extremities | 41 | 2.54.15 | •• | | |
| Hip | 41 | 3.54 (15) | 39 | 3.00 (10) | |
| Femur, upper leg Knee | 3 58 | 1.00(1) | 8 60 | 1.25 (2) | |
| Tibia, fibula, lower leg | 9 | 2.21 (9) 3.11 (16) | 11 | 2.45 (31) 1.91 (8) | |
| Foot, ankle, toe(s) | 74 | 2.12 (10) | 79 | 2.20 (10) | |
| Arteriogram (legs, feet) | 1 | 1.00(1) | ó | 2.20(10) | |
| Venography (legs, feet) | 3 | 2.33 (3) | 2 | 1.00(1) | |
| Any examination of lower extremities | 130 | 3.61 (20) | 138 | 3.41 (38) | |
| Abdomen | | | | • | |
| Abdomen, KUB (i.e., kidney, ureter, bladder) | 19 | 1.05 (2) | 34 | 1.47 (5) | |
| Computed tomography scan, abdomen | 0 | | 1 | 1.00 (1) | |
| Abdominal arteriogram | l | 1.00(1) | 1 | 1.00(1) | |
| Any examination of abdomen | 20 | 1.05 (2) | 34 | 1.53 (6) | |
| | | | | | |
| Gastrointestinal tract | | | | | |
| Upper gastrointestinal series | 83 | 2.07 (13) | 70 | 2.01(8) | |
| Upper gastrointestinal series Colon, barium enema | 52 | 1.52 (5) | 70 46 | 1.43 (4) | |
| Upper gastrointestinal series | | • • | | | |

Table 3 (continued). Numbers of case and control subjects ever exposed to specific radiographic examinations and mean and maximum number of examinations per exposed person*

| | Case s | subjects $(n = 484)$ | Control subjects $(n = 484)$ | |
|--|----------------|---|------------------------------|---|
| Examination | No. exposed | Examinations per exposed person, mean (maximum) | No. exposed | Examinations per exposed person, mean (maximum) |
| Cholangiogram | 32 | 1.09 (2) | 25 | 1.28 (3) |
| Endoscopic retrograde cholangiopancreatography | 2 | 1.00(1) | 0 | _ |
| Any examination of gastrointestinal tract | 120 | 3.40 (25) | 119 | 2.81 (14) |
| Urinary tract | | | | |
| Intravenous pyelogram | 49 | 1.31(3) | 58 | 1.64 (6) |
| Retrograde pyelogram | 2 | 1.00(1) | 3 | 1.00(1) |
| Cystogram | 5 | 1.00(1) | 4 | 1.00(1) |
| Renal arteriogram | 5 | 1.40(2) | 1 | 2.00(2) |
| Other procedure, urinary tract | l | 2.00(2) | 0 | <u> </u> |
| Any examination of urinary tract | 50 | 1.60 (5) | 59 | 1.76(6) |
| Female genital tract | | | | |
| Pelvimetry | 7 | 1.00(1) | 10 | 1.10(2) |
| Hysterosalpingogram | 12 | 1.25 (3) | 5 | 1.00(1) |
| Other | 1 | 1.00(1) | 0 | <u> </u> |
| Any examination of female genital tract | 20 | 1.15(3) | 15 | 1.07 (2) |
| Other/unspecified examinations | 0 | _ | 3 | 1.33 (2) |
| Any type of examination | 369 | 7.96 (67) | 367 | 8.75 (78) |

^{*}Examinations occurring within the 5 years preceding the date of thyroid cancer diagnosis are excluded for case subjects and matched control subjects.

those exposed. Examinations of particular interest with regard to potential for exposure to the thyroid gland include those of the neck, upper spine, skull, face, upper gastrointestinal tract, and chest. There was no consistent pattern of case subjects having had more of the types of x-ray procedures associated with higher dose to the thyroid than control subjects. The most common procedures were x rays and photofluorographs of the chest. One case subject had 23 chest x rays, and one control subject had 68 chest x rays. There were more chest x rays among case subjects but more photofluorographs among control subjects. More case than control subjects had received x rays of the jaw and of soft tissues in the neck. Slightly higher percentages of case subjects had received an examination of the thoracic spine or upper gastrointestinal series. Relatively more control subjects, however, had received x rays of the nose, sinuses or face, shoulder, and scapula. Case and control subjects had similar numbers of x-ray examinations of the cervical spine, full spine,

The usual reason for the x-ray examinations of soft tissues of the neck was goiter or suspicion of goiter. Twenty-three of 44 case subjects and seven of 18 control subjects for whom reason for referral for x-ray examination was known were given the examination to confirm or rule out a clinical diagnosis of goiter. The clinical diagnosis was confirmed by the x ray in 21 case subjects and six control subjects. Indications for the x rays among the remaining case and control subjects were either pain or discomfort or difficulty in swallowing; in none of these instances did the x ray reveal a goiter as the underlying cause.

With regard to examinations of parts of the body more distant from the neck area, which would have resulted in very small doses to the thyroid, some procedures were more common among case subjects and others were more common among control subjects. This situation is as one might expect if differences were attributable primarily to chance. Examination of results separately for males versus females and for papillary versus follicular cancers did not reveal other notable case—control differences.

Tables 4 and 5 present results separately by calendar year and age at exposure, respectively, for groupings of x-ray procedures corresponding to presumptive high (i.e., in years prior to 1960), medium (in years 1960-1969), and low (in years 1970-1987) exposures. There was no tendency for case subjects to have had more x-ray examinations than control subjects in earlier calendar years. The mean numbers of x-ray examinations before age 20 also were similar for case subjects and matched control subjects.

There was no association between thyroid cancer and numbers of x-ray examinations of the head, neck, or upper spine (Table 6). In addition, there was not a statistically significant trend in the RR for thyroid cancer with increases in the estimated cumulative dose from all medical diagnostic x rays (Table 7). The highest quartile of the cumulative dose distribution corresponds approximately to a thyroid dose of 10-80 mGy, or 1-8 cGy. The mean overall estimated cumulative dose was 5.9 mGy for case subjects and 5.7 mGy for control subjects. These figures include persons for whom the medical record review identified no x rays. If we underascertained x-ray procedures, the actual doses would have been somewhat higher. The excess RR, based on a straight-line dose–response model, was 0.02 per cGy (95%CI = -0.11 to 0.15).

For 115 case subjects and 117 control subjects, there was no medical record documentation of diagnostic x rays during the period 5 or more years before the date of thyroid cancer diagnosis. Of these persons, telephone interviews were completed for 27 case subjects and 23 control subjects. Abstract data were compared with data obtained through the telephone interview,

[†]The x rays were done for medical, not dental, reasons.

Table 4. Average numbers of x-ray examinations of different parts of the body for case and matched control subjects, separately by decades m which examinations occurred*

| | | | Mean No. | of radiographic | examinations per | individual | | |
|-----------------------|---------------|------------------|------------------|---------------------|------------------|------------------|------------------|------------------|
| <1960 | | 1960 | 1960-1969 19 | | -1987 | All years† | | |
| Part of body examined | Case subjects | Control subjects | Case subjects | Control subjects | Case subjects | Control subjects | Case subjects | Control subjects |
| - | | | | | | | | |
| | | | | | | | | |
| Total (entire oddy) | 0.00 | 0.00 | .,,,, | 2.20 | 5.50 | 5.72 | 0.07 | 0.05 |

^{*}Examinations occurring within the 5 years preceding the date of thyroid cancer diagnosis are excluded for case subjects and matched control subjects.

Table 5. Average numbers of x-ray examinations of different parts of the body for case and matched control subjects, separately by age interval*

| | r | Mean No. of radiographic examinations per individual | | | | | | | |
|--|------------------|--|------------------|------------------|------------------|---------------------|--|--|--|
| | Age | Age <20 y Age | | ≥20 y | All ages† | | | | |
| Part of body examined | Case subjects | Control subjects | Case subjects | Control subjects | Case subjects | Control subjects | | | |
| Head, neck, upper spine | 0.06 | 0.04 | 0.57 | 0.58 | 0.62 | 0.61 | | | |
| Chest, shoulders, upper gastrointestinal tract | 0.22 | 0.20 | 2.77 | 3.08 | 2.92 | 3.20 | | | |
| Abdomen, pelvis, arms, legs | 0.28 | 0.25 | 2.30 | 2.64 | 2.53 | 2.82 | | | |
| Total (entire body) | 0.56 | 0.49 | 5.64 | 6.30 | 6.07 | 6.63 | | | |

^{*}Examinations occurring within the 5 years preceding the date of thyroid cancer diagnosis are excluded for case subjects and matched control subjects.

Table 6. Relative risk (RR) of thyroid cancer by numbers of x-ray examinations of different parts of the body*

| Part of body examined | Relative dose to thyroid† | No. of x rays | No. of case subjects | No. of control subjects | RR‡ | 95% confidence interval | P for trend‡ |
|--|---------------------------------|------------------|----------------------|-------------------------|------|-------------------------------|--------------|
| Head, neck, upper spine | Highest | 0 | 349 | 345 | 1.00 | Reference | .54 |
| | | 1-5 | 126 | 131 | 1.02 | 0.76-1.38 | |
| | | ≥6 | 9 | 8 | 1.22 | 0.46-3.34 | |
| Chest, shoulders, upper gastrointestinal tract | Medium | 0 | 157 | 159 | 1.00 | Reference | .50 |
| | | 1-5 | 244 | 240 | 1.06 | 0.78-1.46 | |
| | | 6-10 | 63 | 62 | 1.11 | 0.67-1.87 | |
| | | >10 | 20 | 23 | 0.99 | 0.47-2.08 | |
| Abdomen, pelvis, arms, legs | Lowest | 0 | 254 | 225 | 1.00 | Reference | .42 |
| | | 1-5 | 153 | 182 | 0.75 | 0.56-1.00 | |
| | | 6-10 | 49 | 44 | 0.99 | 0.60-1.62 | |
| | | >10 | 28 | 33 | 0.75 | 0.42-1.35 | |

^{*}Examinations are grouped in terms of their relative radiation dose to the thyroid gland; x rays occurring within the 5 years preceding the date of thyroid cancer diagnosis are excluded for case subjects and matched control subjects.

so that we might assess possible underascertainment associated with the abstraction process. Four case subjects and four control subjects reported no x rays. An additional 18 case subjects and 13 control subjects reported having received one to three x rays, and five case subjects and six control subjects reported having

had four or more x rays. As expected, most of the discrepancy was due to photofluorographic examinations of the chest, which were reported by 18 case subjects (67%) and 16 control subjects (70%), and mammograms. which were reported by five case subjects (19%) and five control subjects (22%). Several persons

[†]The mean number of examinations for all years combined does not equal the sum of the means for each time interval because means for each interval are based on study subjects alive during that interval. For example, persons born after 1959 are not included in the calculation for the interval "<1960."

[†]The mean number of examinations for all ages combined does not equal the sum of the means for each age group because the means for age >=20 years do not include persons under age 20 at the time of thyroid cancer diagnosis.

[†]Assignment of specific x-ray examinations to high, medium, or low dose category was based on dose measurements given by Bengtsson et al. (17) and Kereiakes and Rosenstein (18) (Table 1).

[‡]Adjusted for numbers of x rays in the other two relative dose categories.

Table 7. Distribution of case and control subjects by estimated cumulative radiation dose to thyroid gland from diagnostic x-ray examinations, excluding the 5 years before thyroid cancer diagnosis

| | Cumulative dose group* | | | | | | |
|-------------------------|------------------------|-------------|-------------|-------------|--|--|--|
| | 1† | 2 | 3 | 4 | | | |
| Case subjects | 133 | 116 | 114 | 121 | | | |
| Control subjects | 137 | 114 | 114 | 119 | | | |
| Relative risk‡ | 1.00÷ | 1.05 | 1.04 | 1.05 | | | |
| 95% confidence interval | ÷ | (0.73-1.52) | (0.70-1.55) | (0.73-1.52) | | | |

^{*}Dose groups are ordered from low (1) to high (4). Categories are defined by quartiles of distribution of cumulative dose among control subjects. The approximate range (and mean values) of thyroid doses in the four cumulative dose groups were as follows: category 1, 0.00-0.00 cGy (0.00 cGy); category 2, 0.003-0.16 cGy (0.08 cGy); category 3, 0.17-0.68 cGy (0.32 cGy); category 4, 0.70-7.53 cGy (1.95 cGy).

also reported having received x rays of the arms or legs secondary to trauma, none of which would have had much of an influence on thyroid dose.

The only information available about dental x rays was from

[†]Reference category; estimated dose from diagnostic x rays equals zero.

 $[\]ddagger P$ for trend = .80.

goiter cannot be ruled out. In any case, results are strongly at odds with the suggestion that scatter radiation from diagnostic x rays of parts of the body remote from the thyroid gland increases the risk of thyroid cancer (9).

The radiation dose–response relationship could be evaluated only semiquantitatively, because it was not possible to accurately estimate cumulative dose to the thyroid gland from all x-ray procedures combined for individual people. Some degree of misclassification of thyroid doses is certain to have occurred, and this would have made it difficult to detect a small radiation effect. No evidence of an association between diagnostic irradiation and risk of thyroid cancer was seen, however, either on the metric of cumulative dose or that of number of procedures. These negative findings are not surprising in light of the magnitude of doses. Even with allowance for a degree of underascertainment, the most highly exposed individuals appear to have received doses to the thyroid that were of the same order of magnitude as experienced from natural background sources over the course of a lifetime, about 70 mSv, or 7 cGy (2). The observed RR for the 1-8 cGy group in the present study was 1.05, and the excess RR was estimated as 0.02 per cGy with a 95% CI upper bound of 0.15 per cGy. While it is unclear whether there was any radiation effect in the present study, the data are compatible with the range of excess RR estimates reported in the literature (0.04-0.35/cGy) (15). Values toward the higher end of this range tended to be for exposures occurring during childhood (15).

The absence of a demonstrable effect might be attributable not only to the generally small thyroid doses from diagnostic radiography, but also to the fractionated and protracted nature of the exposure. Studies linking thyroid cancer to prior irradiation generally have involved relatively high dose and high dose rate exposures (15). Protraction of exposure would allow more time for repair mechanisms to operate and, possibly, result in less cancer induction relative to the same dose given briefly (15). Other large-scale studies of thyroid cancer or modularity following exposure to high-dose diagnostic ¹³¹I (22) or living in areas of high background radiation (29) have failed to find evidence of increased risks, possibly because of the low dose rates involved.

Although results from the present study do not support the view that medical diagnostic radiography is an important cause of thyroid cancer, they leave open the possibility that there is a small risk associated with examinations of the jaw, mouth, or neck, possibly contingent on the specific projections used, as well as the number of exposures. Very few persons in the present study received x-ray doses to the thyroid gland in excess of 2 cGy, so results do not bear directly on risk among persons with exceptionally high exposures to diagnostic radiation. Furthermore, we did not have documented histories of dental x rays and so could not assess this type of exposure in a way that was immune from deficient or biased recall. More case subjects than control subjects reported having had full-mouth or Panorex dental examinations, but the reverse was true for bite-wing examinations.

A recent analysis of thyroid cancer incidence among atomic bomb survivors underscores the importance of age at exposure (30). Data from that study indicate that the risk of radiation-in-

duced thyroid cancer is low for exposures occurring in adult-hood but that the risk is much greater for exposures among children. In the present study, there was little evidence of case—control differences even for x-ray examinations given before age 20 (Table 5), but the number of x rays among children and adolescents was small (Table 2). At the same time, the low risk of radiation-induced thyroid cancer in adult atomic bomb survivors gives further reason to believe that risks due to diagnostic radiography in adulthood are minimal.

The approach used for ascertaining diagnostic x rays in this study of thyroid cancer could be applied to studies of other cancers, such as childhood leukemia. Whereas the thyroid gland is within the irradiated field for relatively few x-ray procedures, the active (red) bone marrow is exposed to radiation in varying degrees from many types of examination. The cumulative dose to the bone marrow from diagnostic radiography would be higher than that to the thyroid gland. A previous study of leukemia among members of a prepaid health plan did not find an association between diagnostic x rays and leukemia (13), but only leukemias occurring among adults were included in that study.

In light of the inability to rule out the possibility of cancer risks associated with diagnostic radiography, efforts should continue to be discriminating in the use of x rays and to avoid their use when there is no likely clinical benefit (31). Similarly, the use of shielding and implementation of advancements in equipment and techniques that provide high-quality images while delivering low doses to the patient (32) are to be encouraged. It also should be noted, however, that studies relying on prospectively recorded information about diagnostic x-ray procedures, rather than on the memories of study subjects or their proxies, have failed to find an association with either thyroid cancer or leukemia (12,13). Only for multiple myeloma, a cancer not associated with radiation exposure among survivors of the atomic bomb explosions (33), has a positive association with diagnostic x-ray exposure as ascertained from medical records been reported (13). Although it would be irresponsible to presume the cancer risks of modern radiography to be zero, they certainly appear to be very small—smaller than many risks that people commonly accept in everyday life (34).

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Notes

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Journal of the Nation ARTICLES 1621